Characteristics and treatment outcomes of 69 cases with early prosthetic joint infections of the hip and knee

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Abstract: Purpose: Early prosthetic joint infection (PJI) can be treated with an intensive surgical debridement and implant retention (DAIR) of the prosthesis if (1) the prosthesis is stable, (2) the pathogen is not a difficult-to-treat microorganism, (3) symptoms have lasted for <3 weeks and (4) a sinus tract is absent. Methods: We retrospectively evaluated the treatment outcome of early PJI in the hip and knee in a single orthopaedic centre. An early PJI was defined as a prosthesis infection within 3 months after primary implantation or revision surgery for a non-infectious cause. Results: We identified 69 patients with confirmed early PJI, with a median age of 71 (range 33-84) years. Only 64 % presented with 2 acute signs of infection. The most commonly isolated bacteria were coagulase-negative staphylococci (38 %) and Staphylococcus aureus (25 %). Surgical procedures included DAIR (50 cases, 69 %) and two-stage exchange (19 cases, 31 %). At last follow-up, five of remaining living 67 patients (7.5 %) had a relapse of infection. The overall relapse-free survival of the prosthesis after 2 years was 92.3 % (95 % confidence interval 82-97 %) with no significant difference between DAIR and exchange of prosthesis. Conclusion: Our data suggest that an early PJI should be treated with DAIR as a less invasive procedure whenever possible according to the established treatment algorithm.

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CHARACTERISTICS AND TREATMENT OUTCOME OF 69 CASES WITH EARLY PROSTHETIC JOINT INFECTIONS OF HIP AND KNEE

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Abstract

Purpose. Early prosthetic joint infection (PJI) can be treated with an intensive surgical debridement and implant retention (DAIR) of the prosthesis if 1) the prosthesis is stable, 2) the pathogen is not a difficult to treat microorganism, 3) symptoms have lasted for less than 3 weeks, and 4) a sinus tract is absent.

Methods. We retrospectively evaluated the treatment outcome of early PJI in hip and knee in a single orthopaedic centre. An early PJI was defined as a prosthesis infection within 3 months after primary implantation or revision surgery for a non-infectious cause.

Results. We found 69 cases with confirmed early PJI with a median age of 71 (range 33-84) years. Only 64% presented with ≥ 2 acute signs of infection. The most commonly isolated bacteria were coagulase-negative staphylococci (38%) and *Staphylococcus aureus* (25%). Surgical procedures included DAIR in 50 (69%) and two-stage exchange in 19 (31%). At last follow up, five of 63 patients (7.9%) had a relapse of infection. The overall relapse free survival of prosthesis was 92.3% (95%, CI 82-97%) with no significant difference between DAIR and exchange of prosthesis.

Conclusion. Our data suggest treating an early PJI with DAIR as a less invasive procedure whenever possible according to the established treatment algorithm.

Introduction

A periprosthetic joint infection (PJI) is a medical problem that is rising in importance worldwide because of increased usage of artificial joints [1]. PJI can be caused by direct inoculation of bacteria to the implant or by haematogenous seeding [2]. In the former case, bacteria from the commensal skin flora around the surgical site or from contamination by the health-care provider are introduced to the implant during or soon after surgery. The widest accepted classification of PJI proposed by a group from the Mayo clinic distinguishs between a stage one (or early) in which the infection occurs in the first 3 months after surgery, a stage two (or delayed) in which the infection occurs between 3 and 24 months after surgery and presents typically more indolent with a pain-free interval, and a stage three (or late) which includes infections that occur after 2 years and that are frequently caused by haematogenous dissemination of microbial pathogens [3, 4]. Based on this classification, in 2004 Zimmerli et al. have proposed an individual treatment algorithm for each stage to attain a high success rate with the least invasive surgical procedure [2]. Briefly, a delayed infection always needs an exchange of the prosthesis, whereas early (onset less than 3 months postoperative) or haematogenous infection can be cured by debridement and retention of the prosthesis provided that (i) the prosthesis is stable, (ii) the duration of symptoms does not exceed three weeks, (iii) there is intact skin and soft tissue, and (iv) the causative pathogen is susceptible to a biofilm active antibiotic [2].

Recently, there has been intensive discussion about the optimum period of time after surgery that defines an early infection. Definitions range between two weeks and three months [2, 3, 5-7]. Furthermore, there is a wide range in definition of time (between 8 and 30 days) concerning the maximum duration of clinical signs and symptoms after which a debridement and retention (DAIR) approach may still lead to a successful outcome [8, 9]. In the recently published IDSA guidelines by Osmon et al. a DAIR strategy is recommended (evidence grade 2A) if infectious symptoms occur early within 30 days postoperatively or if length of symptoms is less than 3 weeks [7]. Herein, we retrospectively analysed the characteristics and outcome of early PJI in a 5-year cohort of hip and knee arthroplasties in a single centre. Since our centre defined an early PJI within 3 months postoperatively [2], we had the opportunity to investigate if there was any difference in outcome after DAIR if the definition of an early PJI was shortened from 3 months to one month. We speculated that patients with an early PJI not only present with typical acute inflammatory signs

and symptoms. Furthermore we attempted whether there was a difference in the clinical outcome of PJI if signs and symptoms last longer than 3 weeks until a surgical procedure was performed.

Materials and Methods

Study design and population.

The Schulthess Clinic Zurich is a specialized 160-bed orthopaedic centre with a high rate of surgical interventions (7491 inpatient and 1221 outpatient treatments documented in 2012; 804 primary hip and 579 knee arthroplasties). We retrospectively reviewed all early postoperative exogenous types of infection after a knee or hip prosthesis implantation (either after primary arthroplasty or revision surgery) presenting in the Schulthess Clinic between January 2005 and June 2010. Clinical information on infection was retrieved from the prospectively managed database on all PJI from the Infectious Diseases Clinical Consulting Service and from the hospital information system managed by the Schulthess Clinic in Zurich. Patients with a delayed infection (onset of symptoms 3 to 24 months after the last surgery) as well as patients with an incomplete follow-up were excluded.

Definitions

Prosthetic joint infection (PJI) was diagnosed, if one or more of the following criteria were fulfilled: (i) visible purulence of a preoperative aspirate or intraoperative periprosthetic tissue (as determined by the surgeon), (ii) presence of a sinus tract communicating with the prosthesis, (iii) microbial growth in a preoperative joint aspirate, intraoperative periprosthetic tissue or sonication fluid of the removed implant [2, 7]. As a very early prosthetic joint infection we defined a prosthesis infection with symptom onset ≤ 1 month after primary or revision surgery of knee or hip prosthesis [2] and an early manifestation ≥ 1 and ≤ 3 months. In case of a non-healing wound discharge postoperatively we defined the onset of symptoms 14 days after the surgical operation. If an infection was diagnosed with a revision surgery due to wound discharge or postoperative hematoma within 14 days, the date of the revision operation was defined as the onset of symptoms.

PJI symptoms were divided in $\geq$ or <2 typical acute inflammatory signs (such as pain, purulent wound discharge, erythema, swelling/induration or warmth of the joint, optionally fever), chronic symptoms such

as sinus tract, or other non-specific signs such as, hematoma, joint effusion or luxation, or elevated inflammatory serum biomarker only.

Surgical and antibiotic treatment of early infection

The surgical approach was individually determined at the surgeon's discretion in discussion with the Infectious Disease Consulting Service. There were mainly three potential approaches: (i) debridement antibiotics and implant retention (DAIR), (ii) one- or two-stage exchange of the implant, or (iii) resection arthroplasty. If only parts of the prosthesis were removed, we considered the surgical procedure as a DAIR. For the best outcome with a DAIR, orthopaedic surgeons always went for an arthrotomy instead for an arthoscopy for a better infection control and for cultivating bacteria originating from biofilm and not planktonic bacteria. During the study period, exchange of all mobile parts, type of lavage, and second look surgeries was individually determined at the surgeon's discretion.

The duration of antibiotic treatment was planned either for 3 months in case of patients with hip prosthesis, or for 6 months for patients with knee arthroplasty as recommended in guidelines [7]. An initial intravenous therapy of at least 14 days was planned [2, 7].

Outcome evaluation

Follow-up visits were performed at the outpatient Department of Schulthess Clinic. The patients were followed up for relapse of infection, new infection or death. We defined a relapse of infection if: (i) signs and symptoms of a persistent infection (i.e. communicating sinus tract with the prosthesis) were present after 21 days of an adequate surgical and antibiotic treatment, and/or (ii) the same pathogen either as a monobacterial or polymicrobial infection was re-isolated within 2 years after infection diagnosis, and/or (iii) if death was directly related to the PJI diagnosis [10-13]. Patients who died early due to the sequela of a sepsis (e.g pneumonia) or late to any illness were not defined as relapses. A revision operation within 21 days after the first therapeutic surgical procedure was not considered as a relapse. The most invasive surgical approach was reported as the definitive surgical treatment. A new infection was defined as a PJI at the same anatomical site with isolation of a different microbial pathogen. Cases of death were allocated to infection or non-infection related. Successful response was postulated if the patient had no signs and symptoms of relapse and was not receiving suppressive antibiotic treatment after a follow up period of at least 24 months.

Statistical analysis

GraphPad Prism 6 software (GraphPad, San Diego, CA) was used for statistical calculations and performing figures. The probability of relapse-free survival and the 95% confidence interval (95% CI) was estimated using the Kaplan Meier survival method. Cox proportional hazard analysis was used for comparison of relapse free survivals of different surgical subgroups. Observations were censored at the time of diagnosis of infection relapse. Categorical variables were compared by the chi-square test or Fisher's exact test.

Results

Baseline characteristics

Between January 2005 and June 2010, 864 patients with a possible PJI of the knee (n = 456) or hips (n = 408) treated at the Schulthess Clinic in Zurich were documented in the databank of the Infectious Disease Service. Seventy-five (8.7%) patients of these presented in the early postoperative period within 3 months after surgery. Six patients were excluded because of an incomplete follow-up, so that 69 early infections were further analysed (28 knee, 41 hip prostheses). Characteristics of all 69 patients are summarized in table 1. The left side of the hip or knee joint was more affected by an early infection (60.9% vs. 39.1%).

Symptoms

The median time between the last surgical procedure and onset of symptoms of infection was 14 days and until diagnostic and therapeutic surgical intervention for infection 22 days (table 2). In 58 of 69 cases (84%) first symptoms of infection manifested within 30 days, in 11 cases (16%) between 30 and 90 days. In 60 of 69 patients (87%), symptoms lasted less than 3 weeks until a diagnostic and therapeutic surgical revision for infection was performed.

Forty-four patients (64%) showed ≥2 typical acute inflammatory symptoms such as pain, erythema, wound discharge, swelling/induration, or local warmth of the joint (table 2 and 3). Fifteen of these patients also developed fever, 10 of them with positive blood cultures, two died due to sepsis. Only one inflammatory sign of infection was documented in twelve (17%), signs of a chronic infection such as sinus tract in five patients. In eight patients, non-inflammatory signs and symptoms such as haematoma,

joint effusion or luxation, or elevated inflammatory serum biomarker only were the leading symptoms of the infection.

Diagnostic procedure

In the majority (67 of 69) of patients, microbial growth was detected preoperatively and/or intraoperatively. The two patients with culture negative PJI showed highly infection-suspicious intraoperative signs according to the orthopaedic surgeon, but were treated with antibiotics for 3 days and 20 days, respectively. The mean number of intraoperatively retrieved tissue biopsies was 5.6 (range 2-11) in order to facilitate the differentiation between causing pathogen and contaminants. Most commonly isolated microorganisms were *S. aureus* (17, 38%) and coagulase-negative staphylococci (26, 25%) with methicillin resistance in 1 of 17 (6%) and 24 of 26 (92%), respectively (table 3). Many virulent microorganisms, such as *Staphylococcus aureus, Streptococcus pyogenes*, *S. agalactiae*, *S. dysgalactiae* subsp. *equisimilis*, or *Bacillus cereus,* presented with acute clinical manifestation, whereas many patients with low-virulent pathogens such as coagulase-negative staphylococci, *Enterococcus faecalis,* or *Propionibacterium acnes* presented with delayed (sinus tract) or nonspecific symptoms (table 3).

Antibiotic treatment

The median time of antibiotic treatment was 3.1 months for hip and 6.1 months for knee PJI (table 2), calculated for all patients including the 2 cases with early death due to sepsis at day 9 and 27. Initial intravenous therapy was performed for at least 14 days in 56 of 69 cases (81%). Antimicrobial treatment was chosen according to susceptibility testing of the pathogen with an initial empirical treatment consisting of an intravenous broad-spectrum beta-lactam antibiotic in combination with rifampin. In two patients with a culture-negative PJI, intravenous empirical treatment was followed by an oral treatment with a fluoroquinolone (ciprofloxacin or levofloxacin) and rifampin. In patients with a *Staphylococcus* species or *Propionibacterium acnes* PJI, a rifampin-combination regime was given as a potent antimicrobial substance against bacteria in biofilm [14, 15]. The infectious diseases consultant chose the combination antimicrobial drug according to antimicrobial susceptibility testing (preferably a fluoroquinolone) to avoid emergence of rifampin resistance [16].

Surgical treatment

In the majority of patients (n=50, 72.5%), DAIR of the prosthesis as the most invasive procedure was performed. In 15 of these 50 patients (30%), a second-look operation with a repeated DAIR was done within 2 to 18 days (median 6 days) due to hematoma (n=1), wound discharge (n=10), or routinely (n=4). In all but one (*S. aureus,* intervention at day 6*)*, intraoperative tissue biopsies at second look were negative. These cases with repeated DAIR were not interpreted as treatment failure because of intervention within 21 days after the initial surgical process.

In 19 patients (27.5%), a complete two-stage exchange of the prosthesis was chosen, thereof in seven patients after an initial DAIR within 20 days (median 14, range 6 to 20 days). Reason for an exchange were (i) symptoms lasting for longer than 3 weeks (n=4), (ii) diagnosis of a rifampin-resistant staphylococcus (n=1), (iii) hepatopathy with intolerance to rifampin in case of a staphylococcal PJI (n=1), or (vi) severely damaged periprosthetic tissue (n=13). No resection arthroplasty or one-stage exchange of the prosthesis was performed. In case of a two-stage prosthetic exchange, the median time between removal and replacement was 3.4 months (range 0.5 to 14.9 months).

Outcome analysis

Two patients died due to sequelae of sepsis caused by *S. epidermidis* at day 9 and day 27 postoperatively. At last follow-up 62 of 67 remaining patients were free of infection (median 3.1 years, range 0.2-6.5 years) and five had a relapse of infection (median time to relapse 0.6 years, range 0.2 -0.9 years) with isolation of the same microorganism (n = 3) or a persistent wound discharge or sinus tract > 3 weeks under continuous antibiotic treatment (n = 2). Causing pathogens were methicillin-resistant *Staphylococcus epidermidis* (n = 3), methicillin-susceptible *S. aureus* (n = 1) and one mixed infection with isolation of *Proteus mirabilis* and *Enterococcus faecalis*. Two patients died 4 and 11 months after surgery due to a non-infectious reason. In seven cases (11.1%), a new infection with another microorganism was documented.

The relapse-free survival of the prosthesis in 67 patients (69 minus 2 deaths due to sequela of sepsis) was 92.3% (95% CI 82.6-97%) after 2 years (figure 1A). Stratified by surgical procedure, the relapse-free survival of the prosthesis was 91.6% (95% CI 79.2-96.8) for debridement with retention of the prosthesis and 94.2% (95% CI 65-99.2%) for exchange of the prosthesis (figure 1B) after 2 years.

Outcome stratified according to time of manifestation of infection

In 58 of 69 patients (84%) signs of symptoms of infection developed within 30 days after surgery (very early) and in 11 patients (16%) between 30 and 90 days (early). All five relapses occurred in the group with very early manifestation of clinical symptoms (four relapses after DAIR, one relapse after a two-stage exchange of prosthesis)..Among the patients treated with debridement and retention of the prosthesis, no significant difference in cure rate was calculated for patients with onset of symptoms less or more than 30 days after last surgery (Fischer's exact test, p=1).

Outcome stratified according to duration of symptoms

In recent expert recommendations and guidelines (evidence grade 2A), it is recommended to treat a PJI with a DAIR if signs and symptoms have lasted less than 3 weeks [2, 7, 17]. From our 69 patients, nine patients (13%) showed clinical symptoms for more than 3 weeks until a diagnostic and therapeutic intervention was performed. Four of these nine patients (44%) were finally treated with a two-stage exchange, five with DAIR of the prosthesis and two (one treated with DAIR and one with two-stage exchange) developed a relapse of infection. The possible reason for these relapses might have been a persistent biofilm infection due to a remaining screw after complete exchange of the prosthesis and a remaining bone sequester after DAIR.

Among all 60 patients with symptoms less than 3 weeks finally treated with DAIR in 45 and two-stage exchange in five, three patients developed a relapse of infection after DAIR. There was no significant difference in cure rates according to duration of symptoms less or more than 3 weeks (Fisher's exact test, p=0.4).

Discussion

Our retrospective analysis of 69 early infections after implantation of a knee or hip prosthesis shows that only 64% of the patients present with ≥2 acute inflammatory symptoms. *Staphylococcus aureus* (25%), coagulase-negative staphylococci (38%), and Gram-negative bacteria (11.6%), were the most commonly found causative organisms in early PJI. Thus, low virulent pathogens such as coagulase-negative staphylococci quite commonly cause early infection.

Two thirds of the patients with early PJI showed ≥ 2 acute symptoms of an infection such as pain, wound discharge, erythema, swelling/induration or warmth of the joint and/or fever. About one third presented with only one acute inflammatory symptom, or signs of a chronic infection (sinus tract, hematoma, joint effusion/luxation, or elevated inflammatory serum biomarkers only). Typically, early infections are considered to be associated with acute infectious symptoms [2], but still, many patients exclusively suffer from nonspecific symptoms [18]. From our results, we conclude that even in early PJI non-specific symptoms should raise the suspicion of a potential deep prosthetic joint infection and further diagnostic steps such as arthrocentesis and synovial fluid analysis (total and white cell count, microbiological culture) should be enforced. In our study, the most commonly isolated microorganisms were coagulase-negative staphylococci. Thus, these low-virulence microorganisms are not limited to delayed infection.

The goal of treatment in PJI is to cure the infection, prevent its recurrence, and ensure a pain-free and functional joint [19]. Despite the recently published IDSA guidelines on PJI [7], the proposed therapeutic approach is still under debate, since many recommendations are based on non-randomized observational studies and/or expert opinion. There is only one randomized double blinded prospective trial with 33 patients demonstrating that in early staphylococcal PJI, DAIR is a successful treatment provided that a combination of rifampin with a fluoroquinolone (ciprofloxacin) is used [14]. Large cohort studies or randomized controlled trials with high power are still missing. In the US, PJI is traditionally treated with a two-stage exchange, whereas in Europe the approach of extensive debridement, antibiotics, and implant retention (DAIR) is more regularly used. DAIR is favoured if the prosthesis is stable, the pathogen is not a difficult-to-treat microorganism, symptoms have lasted for less than 3 weeks, and skin and soft tissue are intact [2]. For a successful debridement mobile parts of the prosthesis (polyethylene inlay) should be replaced [20, 21], because the lack of removal was shown to be an independent risk factor for treatment failure in an investigation of Choi et al [21]. In general, debridement and retention of the prosthesis is favoured because of a lower morbidity due to a less invasive surgery and reduction of cost due to a shorter hospital stay [22]. Our study showed a successful outcome with a prosthesis survival rate of 92%, without a significant difference between retention and exchange of the prosthesis. These findings support the result of previous published studies in particular the prospective randomized study by Zimmerli et.al studying the

outcome of early staphylococcal infections [14, 23-25]. This study showed a 100% treatment success with DAIR if rifampin was combined with ciprofloxacin and no radiological sign of loosening was detected [2]. Without use of rifampin, treatment success was 58% only. Our study confirmed the good outcome of DAIR treatment with extension to other microbial pathogens than staphylococci. But if patients are not properly selected or if a polymicrobial infection was diagnosed, poorer outcome with debridement and retention was found [11, 12, 26].

In the literature, duration of symptoms was stressed to be an important risk factor for successful debridement and retention [2, 8]. Taking into account the low number of relapses in our study, we could not find any difference between patients treated with DAIR with duration of symptoms of less or more than 3 weeks. The reason for treatment failure in 4 patients with DAIR was (i) suppressive treatment without rifampin from the beginning because of non-adherence (iv-drug use) and liver cirrhosis, (ii) intolerance to rifampin, (iii) polymicrobial infection, and (iv) a remaining bone sequester after debridement. In the one patient with treatment failure after two-stage exchange, a screw for a fixation device remained in situ and could not be removed, which caused persistent infection.

Patients in our study received a long-term antibiotic treatment with a median duration of 3.1 in hip or 6.1 months in knee PJI, which is based on European and American guidelines [7, 27]. A total treatment period of 3 months for hip and 6 months for knee joint infections was recommended earlier [2]. A cohort study from Australia with 147 patients with early PJI recently found that a shortened treatment course for less than 3 months is a risk factor for treatment failure [6]. However, recently published studies favour shorter treatments [28-31], but no randomized controlled trials exist up to now.

No consensus exists on the period of time after surgery that defines an early infection. Definitions range between two weeks and three months [2, 3, 5-7]. In our study, no difference in outcome was seen in patients presenting with very early (≤ 30 days) and early (30-90 days) manifestation of PJI. This underlines the probably more important fact of consequent use of rifampin in staphylococcal infections and choosing DAIR as treatment option only after proper selection of patients with a stable prosthesis.

This study provides important epidemiological and clinical data about early PJI and its treatment possibilities. It especially underlines the good outcome with DAIR in a properly selected cohort of patients and supports the data of a previously randomized controlled study of Zimmerli et al. with extension to a

variety of microbial pathogens. Limitations of the study are the retrospective design and the low number of patients with symptoms longer than 3 weeks or early symptom onset between 30 and 90 days, which did not allow us to perform a risk factor analysis. The studied cohort population was heterogeneous with respect to different isolated pathogens, and because we did not distinguish between primary and revision surgery procedures. This might have led to mistaking a low-grade infection for an early infection after revision surgery in some cases.

In conclusion, our investigation shows that DAIR is not inferior to two-stage exchange of the prosthesis. Therefore, whenever possible according to an established treatment algorithm, early PJI should be treated with DAIR, since it is less invasive. A high cure rate of >90% can be reached with DAIR provided that patients are properly selected, and an experienced multidisciplinary team of orthopaedic surgeons, infectious disease specialists and microbiologists evaluates each case.

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Tables and Figures

Table 1. Baseline characteristics of 69 patients with an early periprosthetic joint knee- (n=28) and hip infection (n=41)

Characteristics	No. of episodes (%)
Median age (years)	71 (33 – 84)
Females	34 (49.3)
Primary implantation of the prosthesis	
Schulthess Clinic	55 (79.7)
External hospital	14 (20.3)
Last surgical procedure before infection	
Primary implantation	37 (53.6%)
Revision surgery	32 (46.4%)
o 1	19
o ≥ 2	13
Localization of joint prosthesis	
Knee	28 (40.6%)
Hip	41 (59.4%)
Left side of implantation	42 (60.9)
Underlying joint disorder	
Degenerative	58 (84)
Posttraumatic	6 (8.7)
Rheumatoid arthritis	4 (5.8)
Osteosarcoma	1 (1.4)
Comorbidity	
Diabetes mellitus	10 (14.5)
Obesity	20 (29.0)
Neoplasia	5 (7.2)
Immunosuppression	12 (17.4)

Table 2. Characteristics of 69 early PJI (knee- n=28, hip n=41)

Characteristics	N (%)
Pathogenesis	
Perioperatively acquired (exogenous)	62 (89.9%)
Hematogenous	7 (11.1%)
Time to manifestation of symptoms (days), median (range)	
Last surgical intervention to onset of symptoms	14 (2 - 68)
Very early presentation (≤ 1 month)	58 (84%)
Early presentation (> 1 month - ≤ 3 months)	11 (16%)
Last surgical intervention to infection diagnosis	22 (2 – 92)
Length of symptoms ≤ 3 weeks	60 (87%)
Length of symptoms > 3 weeks	9 (13%)
Duration of symptoms until surgical management of infection	5 (0 – 78)
Symptoms	
≥2 inflammatory signs and symptoms[a]	44 (64%)
+ fever	15
<2 inflammatory signs and symptoms	12 (17%)
Wound dehiscence or discharge only	8
Persistent pain only	3
Warmth only	1
Sinus tract	5 (7%)
Other signs and symptoms	8 (12%)
Hematoma	3
Joint effusion	2
Joint luxation	2
Elevated inflammatory biomarker only	1

Antibiotic treatment, median months (range)	3.5 (0.3-8.3)
Intravenous (days)	17 (7-126)
Knee, median month (range)	6.1 (1.3-8.3)
Hip, median month (range)	3.1 (0.3-6.7)
Surgical treatment	
Debridement and retention (DAIR)	50 (72.5%)
+ exchange of polyethylene inlay	17
+ exchange of a part of the prosthesis	9
Two-stage exchange of the prosthesis	19 (27.5%)
As the initial surgical approach	12
Within 20 days after initial DAIR	7

313 [a] ≥ 2 manifestation of inflammation such as pain, purulent wound discharge, erythema, swelling/induration
314 or warmth of the joint

315 **Table 3**. Microbiological characteristics with description of signs and symptoms of 69 patients with early PJI

Microbial pathogen	N (%)	N (%)				
	N (%)	≥2 inflammatory signs/symptoms[d]	+ fever	<2 inflammatory signs/symptoms	Sinus tract	Other signs/symptoms[e]
Monobacterial	64 (92.7)	44 (64)	15	12 (17)	5 (7)	8 (12)
Staphylococcus aureus[a]	17	16	6	1	0	0
Coagulase-negative staphylococcus[b]	26	13	0	7	2	4
Streptococcus pyogenes	1	1	0	0	0	0
Streptococcus dysgalactiae subsp. *equisimilis*	1	1	1	0	0	0
Streptococcus agalactiae	2	2	1	0	0	0
Enterococcus faecalis	1	0	0	0	1	0
Bacillus cereus	1	1	1	0	0	0
Escherichia coli[c]	3	2	1	1	0	0
Citrobacter koseri[c]	2	1	0	1	0	0
Pseudomonas aeruginosa[c]	1	0	0	0	0	1
Enterobacter cloacae[c]	1	1	1	0	0	0
Haemophilus parainfluenza[c]	1	0	1	0	0	1

Proteus mirabilis[c]	1	1	0	0	0	0
Propionibacterium acnes	3	1	0	1	0	1
Granulicatella adjacens	1	0	1	1	0	0
Clostridium hastiformis	1	0	1	0	1	0
Candida famata	1	0	0	0	1	0
Polymicrobial[d]	3 (4.4)	2	0	0	0	1
Culture negative	2 (2.9)	2	1	0	0	0

316 [a] Susceptibility testing: n=16 methicillin susceptible, n=1 methicillin resistant

317 [b] Coagulase-negative staphylococci included *S. epidermidis* (n=22), *S. haemolyticus* (n=2), *S. capitis* (n=2); n=24 methicillin resistant, n=2 methicillin

318 susceptible

319 [c] No multidrug-resistant Gram-negative pathogens

320 [d] Polymicrobial infections included: *S. epidermidis*, *P. acnes* (n=1); *Proteus mirabilis, S. aureus, Enterococcus faecalis* (n=1), *S. epidermidis, E. faecalis*

321 (n=1)

322 [e] ≥ 2 manifestation of inflammation such as pain, purulent wound discharge, erythema, swelling/induration or warmth of the joint

323 [e] haematoma, joint effusion or luxation, elevated inflammatory serum biomarker only

324

325 **Table 4.** Relapse of early periprosthetic joint infection (PJI) (n=5)

No.	**Age, sex**	**Joint**	**Infecting organism**	**Time after last surgery (months)**	**Durations of symptoms (days)**	**Surgical treatment**	**Antimicrobial treatment (total duration of treatment)**	**Time to relapse (months)**
1	67, w	Hip	*S. epidermidis, mr*	0.5	1	DAIR	Amoxicillin-clavulanate iv, trimethoprim-sulfamethoxazole po (suppression). No iv treatment	3.1 during suppression medication
2	76, w	Hip	*S. epidermidis, mr*	0.8	1	DAIR, exchange of part of prosthesis	Vancomycin iv/R po, fusidic acid po/R po (3.6 months)	11.8
3	64, m	Knee	Polymicrobial (*P. mirabilis, E. faecalis, S. aureus, ms)*	0.4	1	DAIR	Imipenem-cilastin iv/R po, amoxicillin-clavulanate iv/R po, ciprofloxacin po/R po (6.1 months)	6.7
4	51, w	Hip	*S. aureus, ms*	0.3	44	DAIR. Bone sequester in situ	Flucloxacillin iv/R po, levofloxacin po/R po (4.5 months)	6.6

5	76, w	Hip	*S. epidermidis, mr*	0.	12	Two-stage exchange, screw remained in situ	Daptomycin iv/R po, linezolid po/R po, trimethoprim-sulfamethoxazole po (suppression)	1.8 during suppression

326 R, rifampicin; mr, methicillin resistant; iv, intravenous; po, peroral

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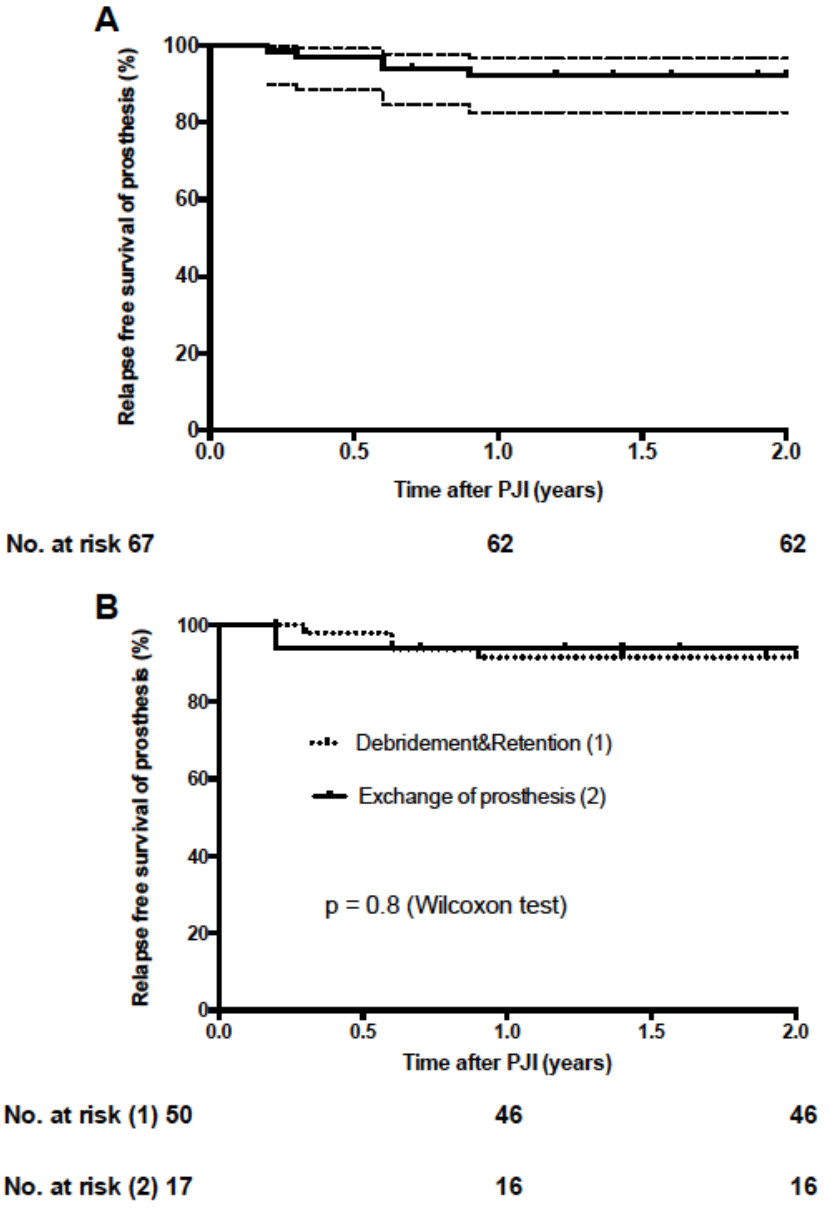
Figure 1. Kaplan Meier curve with relapse free survival of prosthesis in 69 patients **(A)** and stratified, if treatment with a debridement and retention (n=49) or exchange of the prosthesis (n=20) was performed **(B).** In A, dotted lines represent 95% confidence interval (CI). The relapse-free survival of the prosthesis in 67 patients (69 minus 2 deaths due to sepsis) was 92.3% (95% CI 82.6-97%) after 2 years (A). Stratified by surgical procedure, the relapse-free survival of the prosthesis was 91.6% (95% CI 79.2-96.8) for DAIR and 94.2% (95% CI 65-99.2%) for exchange of the prosthesis (B) after 2 years.



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